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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/848,159	05/03/2001	Yang-Dar Yuan	D2977	7424

7590

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EXAMINER

HUI, SAN MING R

ART UNIT

PAPER NUMBER

1617

DATE MAILED: 03/26/2002

Please find below and/or attached an Office communication concerning this application or proceeding.

## Office Action Summary

Applicati n N .

09/848,159

Applicant(s)

YUAN ET AL.

Examiner

San-ming Hui

Art Unit

1617

-- The MAILING DATE of this communication appears on the cover sheet with the corresponding address --  
Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

### Status

- 1) ☒ Responsive to communication(s) filed on 02 October 2001.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

### Disposition of Claims

- 4) ☒ Claim(s) 1-26 is/are pending in the application.
- 4a) Of the above claim(s) 7-10, 13-15 and 17-21 is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 1-6, 11, 12, 16 and 22-26 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

### Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
- Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- 11) ☐ The proposed drawing correction filed on \_\_\_\_\_ is: a) ☐ approved b) ☐ disapproved by the Examiner.
- If approved, corrected drawings are required in reply to this Office action.
- 12) ☐ The oath or declaration is objected to by the Examiner.

### Priority under 35 U.S.C. §§ 119 and 120

- 13) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some \* c) ☐ None of:
- ☐ Certified copies of the priority documents have been received.
  - ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
  - ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- \* See the attached detailed Office action for a list of the certified copies not received.
- 14) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).
- a) ☐ The translation of the foreign language provisional application has been received.
- 15) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

### Attachment(s)

- ☐ Notice of References Cited (PTO-892)
- ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) \_\_\_\_\_
- ☐ Interview Summary (PTO-413) Paper No(s). \_\_\_\_\_
- ☐ Notice of Informal Patent Application (PTO-152)
- ☐ Other: \_\_\_\_\_

### **DETAILED ACTION**

The amendment of claims 5, 25 and 26 filed December 27, 2001 is acknowledged.

The outstanding objection of claims 25 and 26 in the previous office action mailed October 2, 2001 is withdrawn in view of the amendments of the claims filed December 27, 2001.

The outstanding rejection of claim 5 under 35 USC 112, second paragraph, set forth in the previous office action mailed October 2, 2001 is withdrawn in view of the amendments of the claims filed December 27, 2001.

Claims 1-26 are currently pending.

Claims 7-10, 13-15, and 17-21 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected species, there being no allowable generic or linking claim. Claims 1-6, 11, 12, 16, and 22-26 have been examined herein to the extent they read on the elected species, AGN 194310 (also known as 4-[[4-(4-ethylphenyl)-2,2-dimethyl-(2H)-thiochromen-6-yl]-ethynyl]-benzoic acid.

### ***Claim Rejections - 35 USC § 103***

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

Claims 1-6, 11, 12, 16, 22-26 are rejected under 35 U.S.C. 103(a) as being unpatentable over Klein et al. (US Patent 5,776,699) in view of Aberg et al. (Atherosclerosis, 1985; 54:89-97), references of record in the previous office action mailed October 2, 2001.

Klein et al. teaches a group of RAR antagonists broadly, including the elected compound AGN 194310, being useful in inhibiting hypertriglyceride (See particularly Col. 3, line 45-col. 4, line 49; also col. 20, line 67).

Klein et al. does not expressly teach the employment of 4-[[4-(4-ethylphenyl)-2,2-dimethyl-(2H)-thiochromen-6-yl]-ethynyl]-benzoic acid specifically in the method of lowering triglyceride. Klein et al. does not expressly teach the employment of 4-[[4-(4-ethylphenyl)-2,2-dimethyl-(2H)-thiochromen-6-yl]-ethynyl]-benzoic acid to prevent myocardial infarction.

Aberg et al. teaches that elevated serum triglyceride is one of the risk factor of developing myocardial infarction (See particularly page 89, third para.; also page 93, Table 1 and page 95, Table 3).

It would have been obvious to one skill in the art when the invention was made to employ AGN 194310 in a method to lower triglyceride level and prevent myocardial infarction.

One of ordinary skill in the art would have motivated to employ 4-[[4-(4-ethylphenyl)-2,2-dimethyl-(2H)-thiochromen-6-yl]-ethynyl]-benzoic acid in a method of lowering triglyceride level and preventing myocardial infarction because the RAR antagonists of Klein et al. are known to be useful in inhibiting hypertriglyceridemia.

Therefore, employing any RAR antagonists of Klein et al., including 4-[[4-(4-ethylphenyl)-2,2-dimethyl-(2H)-thiochromen-6-yl]-ethynyl]-benzoic acid, would have been reasonably expected to be useful in a method of lowering triglyceride level. Furthermore, it is known that elevated serum triglyceride increases the risk of developing myocardial infarction in patients. Therefore, patients taking 4-[[4-(4-ethylphenyl)-2,2-dimethyl-(2H)-thiochromen-6-yl]-ethynyl]-benzoic acid to lower their serum triglycerides level would be reasonably expected to prevent the development of myocardial infarction.

It is applicant's burden to demonstrate unexpected results over the prior art. See MPEP 716.02, also 716.02 (a) - (g). Furthermore, the unexpected results should be demonstrated with evidence that the differences in results are in fact unexpected and unobvious and of both statistical and practical significance. *Ex parte Gelles*, 22 USPQ2d 1318, 1319 (Bd. Pat. App. & Inter. 1992). Moreover, evidence as to any unexpected benefits must be "clear and convincing" *In re Lohr*, 137 USPQ 548 (CCPA 1963), and be of a scope reasonably commensurate with the scope of the subject matter claimed, *In re Linder*, 173 USPQ 356 (CCPA 1972). In the instant case, examples 1-8 in page 23-31 in the specification have been considered but are not found persuasive as to the nonobviousness of the claimed invention herein because examples 1-6 do not present any comparative data for evaluating the unexpected results over the closest cited prior art. As for examples 7 and 8, the data presented is confusing, for example, in example 7, it is unclear how the monkeys of control groups would have an appreciated serum level of the active (4-[[4-(4-ethylphenyl)-2,2-dimethyl-(2H)-thiochromen-6-yl]-ethynyl]-

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benzoic acid). See Table 2. It is also unclear why the serum level of triglyceride of the controlled group would increase rather than just stay the same. See Table 1. With all the inconsistent data in example 7, one of ordinary skill in the art would not conclude that the administration of 4-[[4-(4-ethylphenyl)-2,2-dimethyl-(2H)-thiochromen-6-yl]-ethynyl]-benzoic acid would unexpectedly lower the serum triglyceride. It is at best inconclusive based on the data presented in example 7 herein. The data in example 8 merely demonstrates the effectiveness of 4-[[4-(4-ethylphenyl)-2,2-dimethyl-(2H)-thiochromen-6-yl]-ethynyl]-benzoic acid. This is seen to be an expected effect based on the cited prior art. No clear and convincing unexpected result is seen.

### ***Response to Arguments***

Applicant's arguments filed October 2, 2001 regarding Klein teaching AGN 194109 being effective in blocking hypertriglyceridemia caused by coadministered retinoids and therefore the claimed invention not being obvious have been fully considered but they are not persuasive. This is because the claims herein do not recite limitations excluding patients whom co-administering the retinoid compounds. Furthermore, AGN 194109 is not the elected compound herein.

In response to applicant's argument that there is no suggestion to combine the references, the examiner recognizes that obviousness can only be established by combining or modifying the teachings of the prior art to produce the claimed invention where there is some teaching, suggestion, or motivation to do so found either in the references themselves or in the knowledge generally available to one of ordinary skill in

the art. See *In re Fine*, 837 F.2d 1071, 5 USPQ2d 1596 (Fed. Cir. 1988) and *In re Jones*, 958 F.2d 347, 21 USPQ2d 1941 (Fed. Cir. 1992). In this case, motivation to combine Klein's teaching with the teaching of Aberg et al. is clearly provided, as discussed in the 35 USC 103 rejection above.

**THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to San-ming Hui whose telephone number is (703) 305-1002. The examiner can normally be reached on Mon 9:00 to 1:00, Tu - Fri from 9:00 to 6:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Minna Moezie, J.D., can be reached on (703) 308-4612. The fax phone numbers for the organization where this application or proceeding is assigned are (703)

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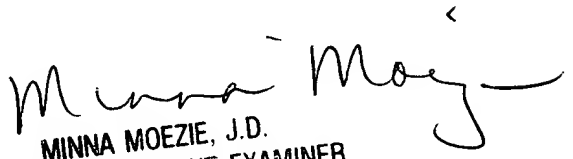
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308-4556 for regular communications and (703) 308-4556 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-1235.

San-ming Hui  
March 24, 2002

  
MINNA MOEZIE, J.D.  
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